UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,925	01/25/2005	Werner Holzl	HM/15-22729/A/PCT	1618

324 7590 08/24/2006

CIBA SPECIALTY CHEMICALS CORPORATION
PATENT DEPARTMENT
540 WHITE PLAINS RD
P O BOX 2005
TARRYTOWN, NY 10591-9005

EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/522,925	HOLZL ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 8-21* is/are rejected.

7)☒ Claim(s) *4-7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included cancellation of claim 2 and amendment to claims 1, 3 and 8-19,filed on 5/12/2006, is made of record. Claims 1 and 321 are pending. In view of applicants' response, 112 second paragraph rejection and 101 rejection of claims 3 and 11-19 have been obviated. In addition, the 112 first paragraph rejection of claims 8 and 9 has been obviated in view of amendment to recite optionally in claim 8. However, method of use claims 10-19 are maintained. Prior art 102 rejections over Kuefner-Muehl and Kelarev are deemed as obviated in view of applicants amendment. However, the following 112 and 103 rejections are now applied necessitated by applicants' amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 8 is indefinite as it now recites R'_3 is a residue of R_3 minus a CH_2 moiety; and R' is a residue of R_3 minus a carbonyl moiety for more than one reason. First of all the "minus" language is vague and unclear. Secondly, it is not clear given the choices of R_3 how would one be able to minus a CH_2. For example, the last choice is a phenycarbonyl and there is no CH_2 in this group. Similarly, the cycloalkylcarbonyl choice has no CH_2 other than those in the ring. Is ring CH_2 to be the group for the

minus. Likewise perfluoro alkyl choice there need not be any CH_2. Even with other choices there are more than one CH_2 and it is not clear which one should be the candidate for minus process.

In addition, not all R_3 choices have a carbonyl group to minus to form R'.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment to claim 8 to recite "R'_3 is a residue of R_3 minus a CH_2 moiety; and R' is a residue of R_3 minus a carbonyl moiety" introduces new matter. The process now requires a reduction of an amide carbonyl of NHCOR' to a $NHCH_2R'$ and elimination of a CH_2 for this reduced group for which there is no support in the specification. The process recited in page 4 of specification does not entail such a deletion. Similarly there is no support for carbonyl minus group. Hence, the present amendment clearly introduces new matter.

Claims 10-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating bacterial infection due to , does not reasonably provide enablement for treating any or all bacterial infection on any or all surfaces and preventing adhesion and formation of biofilms by any or all bacteria

generically embraced in claim 10 and 19 respectively. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

The instant claim 10 and its dependent claim 11-18 are drawn to "antibacterial treatment of surfaces and claim 19 is drawn to "preventing adhesion and formation of biofilms". The scope of the claims includes not only treating or preventing any or all bacterial infections for which there is no enabling disclosure. In addition, the scope of claims include prevention of various bacterial infections such as caused by *Staphylococcus aureus, Cornyebactrium xerosis, Cornyebactrium minuitissimum, Propionibactrium acnes, Proteus vulgaris, Escherichia coli, Klebsiella pneumoniae, Salmonella choleraesuls, Pseudomonas aeruginosa, Candida albicans, Aspergillus niger*. However, specification provides no enabling disclosure showing that all these genus of bacteria can be prevented with the use of the instant compounds. "To prevent" actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Webster's II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the bacterial infection in general claimed herein. Moreover many if not most of bacterial infections such as meningitis, anthrax etc. are very difficult to treat and at present there is no known drug, which can

successfully reverse the course of these infectious diseases, despite the fact that there are many antibacterial drugs, which can be used for "treating bacterial infections". Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1094-1099, 2001, wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of preventing solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Snyder et al., J. Med. Liban 48(4): 208-214, 2000 (PubMed Abstract provided), wherein with regards to antibacterial therapies, it is stated that " common bacteria whose susceptibility to antimicrobials is no longer predictable".

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Antibacterial treatment of surfaces and preventing adhesion and formation of biofilms that require inhibiting activity of instant compound.

2) The state of the prior art: Although there are large number antibacterial agents, none of them are claimed or shown to be useful in treating and or preventing any or all bacterial infections. Recent publication expressed that treating disease by the inhibition of is still exploratory. See Snyder et al. cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds for treating and or preventing any or all bacterial infections on any or all surfaces. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples for treating and or preventing any or all bacterial infections on any or all surfaces and the state of the art is that the effects of bacterial agents based on the disclosed inhibitory activity are unpredictable and at best limited to treating some specific bacterial infection.

6) The breadth of the claims: The instant claims embrace any or all bacterial infections including those yet to be related to like activity.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of receptor-ligand interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards preventing variety of bacterial infections of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

This rejection is same as made in the previous office action. Applicants' traversal to overcome this rejection is not persuasive.

First of all, as recited the claims recite any or all bacteria and any or biofilms. But applicants argued that instant compounds do not have show activity for all bacteria or biofilms but just some. Thus, applicants are admitting that the compounds may not be active against all bacteria or biofilms. This clearly supports the scope of enablement rejection.

Secondly, examples 5-7 prove only the effectiveness of those bacteria tested not any or all bacteria or biofilms. There should be enablement of scope in the specification or prior art. As noted above prior art does not lend support to the notion that any or all bacteria can be treated with a single class of compounds.

As for In re Soni 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), it noted that the rejection clearly recites what is enabled and what is not in the specification. Again, this is a scope of enablement rejection not a total enablement rejection.

As for In re Goffe 191 USPQ 429, 431 (CCPA, 1976), the issue is objective enablement. The court did not say there could be lack of scope of enablement.

As for In re Borkowski, 164 U.S.P.Q 642, 645 (C. C.PA 1970), it is clear that extensive undue experimentation is needed to arrive at which bacteria or biofilm is treatable and which is not. Again, the teachings in specification if not fully enabled for the scope, should provide objective enablement and such is not seen in the prior art.

Hence, this rejection is proper and is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 9 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuefner-Muehl. DE 19735800

Kuefner-Muehl et al., teaches several trisubstituted triazines including the pyridyltriazine compounds useful as adenosine antagonist, which include compounds claimed in the instant claims. See entire document especially page 3, formula I and note the definition of R^1, R^2, R^3 and R^4. Note when R^1 is C_1-C_4 alkyl and C_3-C_7 cycloalkyl, R^2 and R^3 is hydrogen or C_1-C_5 alkyl, R^3 is pyridyl and R^4 is C_1-C_4 alkyl and C_3-C_7 cycloalkyl, compounds taught by Kuefner-Muehl et al., include instant compounds when instant R^2 is hydrogen, R^3 is hydrogen or C_1-C_5 alkyl and R^1 is C_1-C_4 alkyl or C_3-C_7 cycloalkyl. See pages 13 and 14 for process of making which include the process claimed in claim 9. See pages 19 to 45 for various compounds made. Especially see Table 5, examples 104-108 which include instant compound. See also example 3, 4 and 5 for R^2 as alkyl is taught.

While said compounds do not anticipate the scope of instant claims in view of the

present amendment, they are very closely related having NH_2 in the reference versus $NHCH_3$ in the instant claims. However, compounds that differ only in having H vs Me on nitrogen are not deemed patentably distinct absent evidence of superior or unexpected properties. See for compounds that differ only as H vs Me on nitrogen, Ex parte Weston 121 USPQ 428; In re Doebel 174 USPQ 156.

Thus, one skilled in the art at the time of the invention would have been motivated to make compounds that have methyl on the nitrogen and expect the these compounds to possess the utility in the instant case in view of the close structural similarity outlined above.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kelarev et al., Khimiya Geterotsiklicheskikh Soedinenii 5, 674-680, 1988, CA 110: 114800, 1989 (CAPLUS Abstract provided).

Kelarev et al., teaches several substituted pyridyltriazine compounds which include compounds claimed in the instant claims. See the methyl substituted compound in CAPLUS Abstract.

While said compounds do not anticipate the scope of instant claim 1 in view of the present amendment, they are very closely related having NH_2 in the reference versus $NHCH_3$ in the instant claim. However, compounds that differ only in having H vs Me on nitrogen are not deemed patentably distinct absent evidence of superior or unexpected properties. See for compounds that differ only as H vs Me on nitrogen, Ex parte Weston 121 USPQ 428; In re Doebel 174 USPQ 156.

Thus, one skilled in the art at the time of the invention would have been

motivated to make compounds that have methyl on the nitrogen and expect the these compounds to possess the utility in the instant case in view of the close structural similarity outlined above.

Allowable Subject Matter

Claims 4-7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571)

272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson whose telephone number is (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

8/20/2006